

Amendments to the Claims:

Claim 1. (Currently amended) A method for identifying a compound that modulates DAF-18 expression or activity, comprising:

(a) providing a *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell expressing a ~~*C. elegans daf-18*~~ gene that encodes a polypeptide having 95% amino acid sequence identity to SEQ ID NO:310; and

(b) contacting said *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell with a candidate compound to determine the effect of said candidate compound on ~~*C. elegans*~~ said *daf-18* expression or activity, an alteration in said ~~*C. elegans daf-18*~~ expression or activity following contact of said *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell with said candidate compound identifying said candidate compound as a modulatory compound.

Claim 2. (Currently amended) A method for identifying a compound that modulates PTEN expression or activity, comprising:

(a) providing a *C. elegans* or isolated *C. elegans* cell comprising a mutation in its endogenous *daf-18* gene;

(b) expressing in said *C. elegans* or isolated *C. elegans* cell a ~~human~~ PTEN gene that encodes a polypeptide having 95% amino acid sequence identity to SEQ ID NO:309; and

(c) contacting said *C. elegans* or isolated *C. elegans* cell with a candidate compound to determine the effect of said candidate compound on ~~human~~ said PTEN expression or activity, an alteration in said ~~human~~ PTEN expression or activity following contact with said candidate compound identifying said candidate compound as a modulatory compound.

Claim 3. (Currently amended) The method of claim 1 or 2, wherein said compound increases ~~*C. elegans*~~ said *daf-18* or ~~human~~ said PTEN expression or activity and is therefore a candidate compound for increasing longevity of a cell or organism.

Claim 4. (Currently amended) The method of claim 1 or 2, wherein said compound decreases ~~*C. elegans*~~ said *daf-18* or ~~human~~ said PTEN expression or activity and is therefore a candidate compound for treating an impaired glucose tolerance condition or obesity.

Claim 5. (Previously amended) The method of claim 1 or 2, wherein said method is carried out in a transgenic *C. elegans*.

Claims 6-9. (Cancelled)

Claim 10. (Currently amended) A method for identifying a compound that is a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity, comprising contacting a biological sample with a candidate compound and assaying said sample for ~~*C. elegans*~~ DAF-18-mediated lipid phosphatase activity, wherein said DAF-18 has at least 95% amino acid sequence identity to SEQ ID NO:310, a decrease in said activity indicating a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity.

Claim 11. (Currently amended) A method for identifying a compound that is a candidate compound for increasing longevity of a cell or organism, comprising contacting a biological sample with a candidate compound and assaying said sample for ~~*C. elegans*~~ DAF-18-mediated lipid phosphatase activity, wherein said DAF-18 has at least 95% amino acid sequence identity to SEQ ID NO:310, an increase in said activity indicating a candidate compound for increasing longevity of a cell or organism.

Claim 12. (Currently amended) A method for identifying a compound that is a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity, comprising contacting a biological sample with a candidate compound and assaying said sample for ~~human~~ PTEN-mediated lipid phosphatase activity, wherein said PTEN has at least 95% amino acid sequence identity to SEQ ID NO:309, a decrease in

said activity indicating a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity.

Claim 13. (Currently amended) A method for identifying a compound that is a candidate compound for increasing longevity of a cell or organism, comprising contacting a biological sample with a candidate compound and assaying said sample for ~~human~~ PTEN-mediated lipid phosphatase activity, wherein said PTEN has at least 95% amino acid sequence identity to SEQ ID NO:309, an increase in said activity indicating a candidate compound for increasing longevity of a cell or organism.

Claim 14. (Currently amended) The method of claim 10 or 12, wherein said method further comprises assaying said compound in a *C. elegans* or isolated *C. elegans* cell which comprises a mutation in its endogenous *daf-18* gene and which expresses a ~~human~~ PTEN gene which has at least 95% amino acid sequence identity to SEQ ID NO:309, a decrease in ~~human~~ said PTEN activity indicating a candidate compound for treating an impaired glucose tolerance condition or obesity.

Claim 15. (Currently amended) The method of claim 11 or 13, wherein said method further comprises assaying said compound in a *C. elegans* or isolated *C. elegans* cell which comprises a mutation in its endogenous *daf-18* gene and which expresses a

~~human~~ PTEN gene which has at least 95% amino acid sequence identity to SEQ ID NO:309, an increase in ~~human~~ said PTEN activity indicating a candidate compound for increasing longevity of a cell or organism.

Claims 16-22. (Cancelled)

Claim 23. (Currently amended) A transgenic *C. elegans* whose cells contain a transgene encoding a ~~human~~ PTEN polypeptide, said PTEN polypeptide having at least 95% amino acid sequence identity to SEQ ID NO:309.

Claim 24. (Cancelled)

Claim 25. (Previously amended) The transgenic *C. elegans* of claim 23, wherein said *C. elegans* carries a mutation in its endogenous *daf-18* gene.

Claim 26. (Previously added) The method of claim 5, further comprising the step of testing said identified compound in a diabetic or obesity mouse model system.

Claims 27 and 28. (Cancelled)

Claim 29. (New) The method of claim 1, wherein said *daf-18* gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:310.

Claim 30. (New) The method of claim 2, wherein said PTEN gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:309.

Claim 31. (New) The method of claim 3, wherein said *daf-18* gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:310 or said PTEN gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:309.

Claim 32. (New) The method of claim 4, wherein said *daf-18* gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:310 or said PTEN gene encodes a polypeptide having 100% amino acid sequence identity to SEQ ID NO:309.

Claim 33. (New) The method of claim 10 or 11, wherein said DAF-18 has 100% amino acid sequence identity to SEQ ID NO:310.

Claim 34. (New) The method of claim 12 or 13, wherein said PTEN has 100%

amino acid sequence identity to SEQ ID NO:309.

Claim 35. (New) The transgenic *C. elegans* of claim 23, wherein said PTEN polypeptide has 100% amino acid sequence identity to SEQ ID NO:309.

Claim 36. (New) A method for identifying a compound that modulates DAF-18 expression or activity, comprising:

(a) providing a *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell expressing a *daf-18* gene, said *daf-18* gene encoding a polypeptide that (a) has at least 85% amino acid sequence identity to SEQ ID NO:310, (b) has lipid phosphatase activity, and (c) comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site; and

(b) contacting said *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell with a candidate compound to determine the effect of said candidate compound on said *daf-18* expression or activity, an alteration in said *daf-18* expression or activity following contact of said *C. elegans*, isolated *C. elegans* cell, or isolated mammalian cell with said candidate compound identifying said candidate compound as a modulatory compound.

Claim 37. (New) A method for identifying a compound that modulates PTEN expression or activity, comprising:

(a) providing a *C. elegans* or isolated *C. elegans* cell comprising a mutation in its

endogenous *daf-18* gene;

(b) expressing in said *C. elegans* or isolated *C. elegans* cell a PTEN gene, said PTEN gene encoding a polypeptide that (a) has at least 85% amino acid sequence identity to SEQ ID NO:309, (b) has lipid phosphatase activity, and (c) comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site; and

(c) contacting said *C. elegans* or isolated *C. elegans* cell with a candidate compound to determine the effect of said candidate compound on said PTEN expression or activity, an alteration in said PTEN expression or activity following contact with said candidate compound identifying said candidate compound as a modulatory compound.

Claim 38. (New) The method of claim 36 or 37, wherein said compound increases said *daf-18* or said PTEN expression or activity and is therefore a candidate compound for increasing longevity of a cell or organism.

Claim 39. (New) The method of claim 36 or 37, wherein said compound decreases said *daf-18* or said PTEN expression or activity and is therefore a candidate compound for treating an impaired glucose tolerance condition or obesity.

Claim 40. (New) The method of claim 36 or 37, wherein said method is carried out in a transgenic *C. elegans*.



Claim 41. (New) The method of claim 36 or 37, further comprising the step of testing the identified compound in a diabetic or obesity mouse model system.

Claim 42. (New) A method for identifying a compound that is a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity, comprising contacting a biological sample with a candidate compound and assaying said sample for DAF-18-mediated lipid phosphatase activity, wherein said DAF-18 has at least 85% amino acid sequence identity to SEQ ID NO:310, has lipid phosphatase activity, and comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, a decrease in said activity indicating a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity.

Claim 43. (New) A method for identifying a compound that is a candidate compound for increasing longevity of a cell or organism, comprising contacting a biological sample with a candidate compound and assaying said sample for DAF-18-mediated lipid phosphatase activity, wherein said DAF-18 has at least 85% amino acid sequence identity to SEQ ID NO:310, has lipid phosphatase activity, and comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, an increase in said activity indicating a candidate compound for increasing longevity of a cell or organism.

Claim 44. (New) A method for identifying a compound that is a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity, comprising contacting a biological sample with a candidate compound and assaying said sample for PTEN-mediated lipid phosphatase activity, wherein said PTEN has at least 85% amino acid sequence identity to SEQ ID NO:309, has lipid phosphatase activity, and comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, a decrease in said activity indicating a candidate compound for ameliorating or delaying an impaired glucose tolerance condition or obesity.

Claim 45. (New) A method for identifying a compound that is a candidate compound for increasing longevity of a cell or organism, comprising contacting a biological sample with a candidate compound and assaying said sample for PTEN-mediated lipid phosphatase activity, wherein said PTEN has at least 85% amino acid sequence identity to SEQ ID NO:309, has lipid phosphatase activity, and comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, an increase in said activity indicating a candidate compound for increasing longevity of a cell or organism.

Claim 46. (New) The method of claim 41 or 43, wherein said method further comprises assaying said compound in a *C. elegans* or isolated *C. elegans* cell which

comprises a mutation in its endogenous *daf-18* gene and which expresses a PTEN gene, said PTEN gene encoding a polypeptide that (a) has at least 85% amino acid sequence identity to SEQ ID NO:309, (b) has lipid phosphatase activity, and (c) comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, a decrease in PTEN activity indicating a candidate compound for treating an impaired glucose tolerance condition or obesity.

Claim 47. (New) The method of claim 42 or 44, wherein said method further comprises assaying said compound in a *C. elegans* or isolated *C. elegans* cell which comprises a mutation in its endogenous *daf-18* gene and which expresses a PTEN gene, said PTEN gene encoding a polypeptide that (a) has at least 85% amino acid sequence identity to SEQ ID NO:309, (b) has lipid phosphatase activity, and (c) comprises a Cys-(X)<sub>5</sub>-Arg lipid phosphatase active site, an increase in PTEN activity indicating a candidate compound for increasing longevity of a cell or organism.

Claim 48. (New) A transgenic *C. elegans* whose cells contain a transgene encoding a PTEN polypeptide, said PTEN polypeptide having at least 85% amino acid sequence identity to SEQ ID NO:309, having lipid phosphatase activity, and comprising a lipid phosphatase active site.

Claim 49. (New) The transgenic *C. elegans* of claim 47, wherein said *C. elegans*

carries a mutation in its endogenous *daf-18* gene.

Amendments to the Drawings:

Kindly replace Figure 25 with Amended Figure 25, submitted herewith.